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REMARKS

Claims 8-25 are pending and under consideration in this application. All the pending claims currently stand rejected. Claims 10 and 18-25 have been cancelled and claim 8 has been amended. Support for the amendments to claim 8 can be found in the specification at, e.g., page 9, line 9, through page 16, line 7.

No new matter has been added by any of the amendments made herein. After the instant amendments and cancellations have been entered, claims 8, 9, and 11-17 will be pending and under consideration in this application.

35 U.S.C. § 112, first paragraph, rejections (Written Description)

At page 2 of the Office Action, claims 11-17 and 19-25 stand rejected under 35 U.S.C. § 112, first paragraph, as allegedly failing to comply with the written description requirement. The applicant respectfully transverses this rejection.
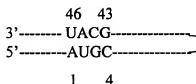
According to the Office Action,

[c]laims 11 and 19...define the term "r" as "one plus the number of nucleic acid bases between said first target region and said complementary region."... However, no clear support has been found for the claimed term "r" being equated to at "one plus the number of nucleic acid bases between said first target region and said complementary region."

The applicant respectfully disagrees and provides the following remarks to show that not only is there ample support for the term "r" being one plus the number of nucleotides between the two complementary sequence regions that form the duplex, but also that, although the wording used to define "r" at page 21 differs from that on page 12 and instant claims 11 and 19, the definitions are (a) not inconsistent with each another and (b) all mean the same thing.

The definition of "r" at page 12, lines 9-10, states that "r is distance between one of double strands and another strand (number of bases between 2 chains (regions) +1))[.]" Thus, "r" is the number of bases between one of the double strands (i.e., a first sequence of a duplex pair) and another strand (i.e., the second sequence of a double strand pair) plus 1. For illustration, consider the hypothetical target mRNA having a first sequence AUGC at positions 1

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to 4 and a second complementary sequence GCAU at positions 43-46, the two sequences

forming the following duplex:

$$
\begin{array}{cc}
46 & 43 \\
3\text{'-------- UACG--------------} \\
5\text{'---------AUGC--------------} \rbrack \\
1 \quad\quad 4
\end{array}
$$

In this case, mathematically, the number of bases between the two regions involved in the duplex

(i.e., the number of bases from position 5 to position 42 of the target mRNA) would be 38.

Adding one, as specified by the definition, would make the value of "r" equal to 39.

Similarly, as defined in claims 11 and 19, "r" is "one plus the number of nucleic acid

bases between said first target region and said complementary target region" (i.e., the number of

bases between the first sequence of the duplex and the second complementary sequence of the

duplex). Using the example target mRNA above, the number of bases between the first target

region and the complementary target region (i.e., the number of bases from position 5 to position

42 of the target mRNA) would be 38 and adding one, as specified by the definition, would bring

the value of "r" to 39.

The applicant respectfully submits that the disclosure at page 12 that defines "r" as "one

plus the number of nucleic acid bases between said first target region and said complementary

region" per se constitutes the necessary written description. Notwithstanding this consideration,

the applicant respectfully submits that, based on the exemplary calculation of "r" on page 13,

line 14, of the specification, the definition of "r" on page 21, lines 6-8, is fully consistent with the

definitions of page 12, lines 9-10, and claims 11 and 19.

Thus, the definition of "r" at page 21 states that "r is expressed as the distance (in terms

of number of bases) between the nearest sites in the substantially complementary chain regions."

In the exemplary calculation on page 13, lines 5-14, of the instant specification, the value of "r"

was obtained by subtracting the residue number of the nearest site nucleotide from one member

of the pair of substantially complementary chains (regions) (as in the definition of "r" on page

21) from the residue number of the nearest site nucleotide of the other member of the pair. The

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value obtained (i.e., 39) by this calculation is exactly the same as that obtained by adding 1 to the number of bases between 2 chains (regions) as "r" is defined on page 12.

Therefore, though the wording for the definition of "r" at page 21 differs from that at page 12 and the claims 11 and 19, the definitions result in the same value for "r."

In view of the above considerations, the applicant respectfully requests that the rejection of claims 11-17 be withdrawn. Since claims 19-25 have been cancelled, their rejection is moot.

35 U.S.C. 112, first paragraph, rejections (Enablement)

At page 4 of the Office Action, claims 8-25 were rejected as allegedly lacking enablement. According to the Office Action,

> [i]n order to use the claimed invention one of skill in the art must assign the numerical values from either step (c) of independent claim 8 or step (h) of independent claim 18 to each nucleotide within all selected pairs of complementary sequences. In performing either step, every nucleotide within said sequences would be assigned the same numerical value and therefore be rendered indistinguishable. For the reasons discussed below, there would be an unpredictable amount of experimentation required to practice the claimed invention.

The applicant respectfully disagrees, and in view of the amendments made herein and the following remarks, submits that once an mRNA sequence is analyzed fully as specified by the instant claims, each nucleotide in a given complementary sequence will have a different characteristic value. Thus, initially, the same numerical value is assigned to every nucleotide in a selected pair of complementary sequences. However, by analyzing all possible pairs of complementary sequences in the target mRNA (or its precursor) and summing all the numerical values obtained for every individual nucleotide in the complementary sequences, each nucleotide in a given pair of complementary sequences is not assigned the same value, and is distinguishable from all other nucleotides in the relevant complementary pair of sequences.

The instant invention is directed to a method of identifying antisense targets in a given mRNA, or its precursor, by determining which sequences are more likely to form intra-molecular double strand regions (duplexes) and which sequences are less likely to form duplexes. This method includes examining the complementarity of a selected first sequence in the mRNA to a selected second sequence and obtaining and assigning a numerical value to the two sequences

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under consideration based on their probability of forming a complementary duplex (e.g., steps

(g) and (h) of claim 8). This process is then repeated with the same first sequence and all other

possible second sequences (step (i)). The whole procedure is then repeated with every possible

first sequence (step (j)). Finally, all of the different values obtained for each nucleotide in the

target mRNA are summed (step (k)). A relatively high summed numerical value indicates a

higher probability of a nucleotide or region (e.g., a sequence of at least 6 nucleotides) forming a

duplex than would a lower scored nucleotide or region.

Thus, unless all the nucleotides in a given duplex were assigned the same score for each

analysis in which they were involved, it is highly unlikely that all the nucleotides in a given

duplex would have the same summed numerical value. Each nucleotide and, more importantly,

each potential sequence of nucleotides (i.e., each region), would have a distinguishable summed

numerical value to describe how likely it is to form a duplex. In view of these above factors, the

applicant respectfully submits that one of ordinary skill in the art could readily distinguish

between regions based on their summed numerical value and would not need to resort to trial and

error experimentation in order to practice the claimed invention.

In light of these considerations, the applicant respectfully requests that the rejections

under 35 U.S.C. § 112, first paragraph, be withdrawn.

35 U.S.C. § 112, second paragraph, rejections (Indefiniteness)

(a) Claims 8-25 stand rejected under U.S.C. § 112, second paragraph, as allegedly indefinite.

At page 7, the Office Action states that

> [c]laim 8 recites the limitation of "selecting all pairs of sequences on the
> target mRNA, or its precursor,…without independently selecting pairs of
> sequences that are shorter than, and composed of nucleotides of, the
> selected sequences"…As such, the instant limitation relies on circular
> logic as a practitioner is required to know what the selected sequences are
> without ever first defining or identifying all pairs of selected sequences.

Although the applicant disagrees with the above characterization, the relevant text of

claim 8 has been deleted, thereby rendering the rejection of claim 8, and any of the claims

dependent therefrom, moot.

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(b)   Claims 8 and 18 stand rejected under 35 U.S.C. § 112, second paragraph, as allegedly

indefinite. At page 8, lines 5-16, the Office Action states,

> [i]t is unclear from the instant claims whether the recitation of terms
> 'region' or 'regions' relate to specific portions of some or all of the
> complementary sequences derived from the target mRNA, or its precursor,
> utilized in the previously recited method steps or if the claimed terms are
> intended to encompass other 'regions' of a sequence consisting of at least
> 6 nucleotides. If applicants intend the terms region or regions to
> specifically refer to portions of the mRNA target sequence selected in the
> preceding method steps, then the claimed limitations further lack proper
> antecedent basis in the instant claim.
>
> ....
>
> For the purpose of continuing examination, the Examiner has construed
> the claimed limitation of a "region" and "regions" to read as one or more
> sequences found within the target mRNA sequence or its precursor as
> recited in steps (a) of claim 8[.]

The applicant respectfully disagrees with the above characterization of claim 8. In light

of the explanation provided below and the amendments made in the interest of enhanced clarity

to step (l) of claim 8, the applicant submits that the terms "region" or "regions" are not

indefinite.

First, although the "region" or "regions" would include nucleotides of the various first

and second sequences selected in method steps (a) and (b) of claim 8, they are not the same as

the first and second sequences. Rather, as defined in method step (l) of claim 8, the terms

"region" or "regions" refer to one or more nucleotide sequences of the target mRNA, or its

precursor, at least 6 nucleotides in length selected by the practitioner of the method because of

their low summed numerical value relative to the summed numerical value of other nucleotide

sequences of the target mRNA, or its precursor. As discussed above, the summed numerical

value for a given region is determined by summing up the values assigned to nucleotides

contained in the region, the values determined by summing values obtained with all possible

pairs of first and second sequences, and then assigned as specified by method steps (a)-(k) of

claim 8.

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The applicant respectfully submits that in view of the above considerations, claim 8 meets the definiteness requirement and asks that its rejection, along with the rejection of its dependent claims, be withdrawn. Claim 18 and its dependent claims (19-25) have been cancelled, thereby rendering their rejection moot.

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CONCLUSION

In summary, for the reasons set forth above, the applicant maintains that the pending claims patentably define the invention. The applicant requests that the Examiner reconsider the rejections as set forth in the Office Action, and permit the pending claims to pass to allowance.

If the Examiner would like to discuss any of the issues raised in the Office Action, the applicant's undersigned representative can be reached at the telephone number listed above.

Please apply any charges or credits to Deposit Account No. 06-1050, referencing Attorney Docket No. 13797-002002.

Respectfully submitted,

Date: 10/5/06

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